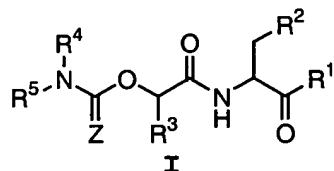


CLAIM AMENDMENTS

Please replace all prior versions and listings of claims with the amended claims as follows:

1-21. (previously canceled)

22. (currently amended) A compound of formula I:



wherein:

Z is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CHN<sub>2</sub>, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y;

R is a C<sub>1-12</sub> aliphatic, aryl, aralkyl, heterocyclyl, or heterocyclylalkyl ring, wherein each of these groups is optionally substituted, and wherein said heterocyclic ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S;

Y is an electronegative leaving group selected from F, Cl, Br, I, arylsulfonyloxy, alkylsulfonyloxy, trifluoromethanesulfonyloxy, OR', SR', -OC=O(R'), or -OPO(R<sup>6</sup>)(R<sup>7</sup>);

wherein R' is an aliphatic group, an aryl group, an aralkyl group, a carbocyclic group, an alkyl carbocyclic group, a heterocyclic group, or an alkyl heterocyclic group;

wherein R<sup>6</sup> and R<sup>7</sup> are independently selected from R or OR;

R<sup>2</sup> is+

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~

ii) ~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl~~

esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters  
thereof; or primary, secondary or tertiary amides  
thereof; wherein suitable substituents on the nitrogen of  
said amides includes one or more C<sub>1-6</sub> alkyl groups  
optionally substituted with N(R)<sub>2</sub>, or 5-6 membered  
heterocyclic rings containing 1-2 heteroatoms; and  
wherein R is linear or branched C<sub>1-12</sub> aliphatic;

R<sup>3</sup> is selected from H, a side chain of a natural  $\alpha$ -amino acid, or a substituted or unsubstituted group having a molecular weight up to about 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl or heterocyclylalkyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and

R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system having 1-6 heteroatoms selected from nitrogen, oxygen or sulfur; wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)R<sup>9</sup>;

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group; wherein the optional substituents on said C<sub>1-12</sub> aliphatic group or aryl, aralkyl, heterocyclyl, or heterocyclylalkyl ring is independently selected from, from halogen, -R<sup>11</sup>, -OR<sup>11</sup>, -OH, -SH, -SR<sup>11</sup>, acyloxy, substituted or unsubstituted Ph or OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>11</sup>, -N(R<sup>11</sup>)<sub>2</sub>, -NHCOR<sup>11</sup>, -NHCONHR<sup>11</sup>, -NHCON(R<sup>11</sup>)<sub>2</sub>, -NR<sup>11</sup>COR<sup>11</sup>, -NHCO<sub>2</sub>R<sup>11</sup>, -CO<sub>2</sub>R<sup>11</sup>, -CO<sub>2</sub>H, -COR<sup>11</sup>, -CONHR<sup>11</sup>, -CON(R<sup>11</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>11</sup>, -SONH<sub>2</sub>, -S(O)R<sup>11</sup>, -SO<sub>2</sub>NHR<sup>11</sup>,

=NHS(O)<sub>2</sub>R<sup>11</sup>, =O, =S, =NNHR<sup>11</sup>, =NNR<sup>11</sup><sub>2</sub>, =N-OR<sup>11</sup>, =NNHCOR<sup>11</sup>, =NNHCO<sub>2</sub>R<sup>11</sup>, =NNHSO<sub>2</sub>R<sup>11</sup>, or =NR<sup>11</sup>; and

wherein each  $R^{11}$  is independently selected from a  $C_{1-12}$  aliphatic group or a substituted  $C_{1-12}$  aliphatic group.

23-35. (previously canceled)

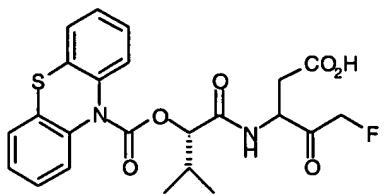
36. (previously amended) The compound of claim 22 wherein the compound is selected from those compounds listed in Table 1 below:

No.	Structure
16	
17	
18	
19	
38	
39	

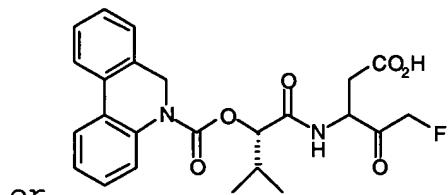


No.	Structure
47	
48	

37. (previously amended) The compound of claim 22 wherein the compound is selected from the following:



12



17

38. (previously canceled)

39. (previously presented) The compound according to claim 22 wherein Z is oxygen.

40. (previously presented) The compound according to claim 22 wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y.

41. (currently amended) The compound according to claim 22 wherein R<sup>2</sup> is-

~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H.~~

CO<sub>2</sub>H, or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic.

42. (previously presented) The compound according to claim 22 wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

43. (previously presented) The compound according to claim 22 wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

44. (previously presented) The compound according to claim 22 wherein Z is oxygen; and wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y.

45. (currently amended) The compound according to claim 22 wherein Z is oxygen; and wherein R<sup>2</sup> is:

- i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H, or~~
- ii) ~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H.~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic.

46. (previously presented) The compound according to claim 22 wherein Z is oxygen; and wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

47. (previously presented) The compound according to claim 22 wherein Z is oxygen; and wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN,

$-\text{NH}_2$ ,  $-\text{NHR}^9$ ,  $-\text{N}(\text{R}^9)_2$ ,  $-\text{NHCOR}^9$ ,  $-\text{NHCONHR}^9$ ,  $-\text{NHCON}(\text{R}^9)_2$ ,  $-\text{NR}^9\text{COR}^9$ ,  $-\text{NHCO}_2\text{R}^9$ ,  $-\text{CO}_2\text{R}^9$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{COR}^9$ ,  $-\text{CONHR}^9$ ,  $-\text{CON}(\text{R}^9)_2$ ,  $-\text{S}(\text{O})_2\text{R}^9$ ,  $-\text{SONH}_2$ ,  $-\text{S}(\text{O})\text{R}^9$ ,  $-\text{SO}_2\text{NHR}^9$ , or  $-\text{NHS}(\text{O})_2\text{R}^9$ ; and wherein each  $\text{R}^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

48. (currently amended) The compound according to claim 22 wherein  $\text{R}^1$  is hydrogen,  $-\text{R}$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{SR}$ , or  $-\text{CH}_2\text{Y}$ ; and wherein  $\text{R}^2$  is:

- i)  ~~$\text{CO}_2\text{H}$ , or an ester, or an amide thereof, or  $\text{R}^2$  is an isostere of said  $\text{CO}_2\text{H}$ , or~~
- ii)  ~~$\text{CH}_2\text{CO}_2\text{H}$ , or an ester, or an amide thereof, or  $\text{R}^2$  is an isostere of said  $\text{CH}_2\text{CO}_2\text{H}$ .~~

$\text{CO}_2\text{H}$ ,  $\text{CH}_2\text{CO}_2\text{H}$  or  $\text{C}_{1-6}$  alkyl esters,  $\text{C}_{3-10}$  cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more  $\text{C}_{1-6}$  alkyl groups optionally substituted with  $\text{N}(\text{R})_2$  or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein  $\text{R}$  is linear or branched  $\text{C}_{1-12}$  aliphatic.

49. (previously presented) The compound according to claim 22 wherein  $\text{R}^1$  is hydrogen,  $-\text{R}$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{SR}$ , or  $-\text{CH}_2\text{Y}$ ; and wherein  $\text{R}^3$  is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclic or heterocyclicalkyl ring wherein said heterocyclic ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

50. (previously presented) The compound according to claim 22 wherein  $\text{R}^1$  is hydrogen,  $-\text{R}$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{SR}$ , or  $-\text{CH}_2\text{Y}$ ; and wherein  $\text{R}^4$  and  $\text{R}^5$  taken together with the intervening

nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

51. (previously presented) The compound according to claim 22 wherein R<sup>2</sup> is:

- i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~
- ii) ~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

52. (currently amended) The compound according to claim 22 wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~  
ii) ~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and

wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

53. (previously presented) The compound according to claim 22 wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and

wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

54. (currently amended) The compound according to claim 22 wherein Z is oxygen;

wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; and wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~  
~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H.~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic.

55. (previously presented) The compound according to claim 22 wherein Z is oxygen;

wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; and wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl

or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

56. (previously presented) The compound according to claim 22 wherein Z is oxygen; wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; and wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

57. (currently amended) The compound according to claim 22 wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H, or~~  
~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H, and~~  
~~CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups~~  
~~optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic~~

rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic;

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

58. (currently amended) The compound according to claim 22 wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~  
~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and~~  
CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and  
wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

59. (previously presented) The compound according to claim 22 wherein  $R^1$  is hydrogen,  $-R$ ,  $-CH_2OR$ ,  $-CH_2SR$ , or  $-CH_2Y$ ; wherein  $R^3$  is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein  $R^4$  and  $R^5$  taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen,  $-R^9$ ,  $-OR^9$ ,  $-OH$ ,  $-SH$ ,  $-SR^9$ , protected OH (such as acyloxy), phenyl (Ph), substituted Ph,  $-OPh$ , substituted  $-OPh$ ,  $-NO_2$ ,  $-CN$ ,  $-NH_2$ ,  $-NHR^9$ ,  $-N(R^9)_2$ ,  $-NHCOR^9$ ,  $-NHCONHR^9$ ,  $-NHCON(R^9)_2$ ,  $-NR^9COR^9$ ,  $-NHCO_2R^9$ ,  $-CO_2R^9$ ,  $-CO_2H$ ,  $-COR^9$ ,  $-CONHR^9$ ,  $-CON(R^9)_2$ ,  $-S(O)_2R^9$ ,  $-SONH_2$ ,  $-S(O)R^9$ ,  $-SO_2NHR^9$ , or  $-NHS(O)_2R^9$ ; and

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

60. (currently amended) The compound according to claim 22 wherein  $R^2$  is:

i)  ~~$CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CO_2H$ ; or~~  
 ~~$CH_2CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CH_2CO_2H$ ,~~  
 ~~$CO_2H$ ,  $CH_2CO_2H$  or  $C_{1-6}$  alkyl esters,  $C_{3-10}$  cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more  $C_{1-6}$  alkyl groups~~

optionally substituted with  $N(R)_2$  or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched  $C_{1-12}$  aliphatic;

wherein  $R^3$  is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein  $R^4$  and  $R^5$  taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen,  $-R^9$ ,  $-OR^9$ ,  $-OH$ ,  $-SH$ ,  $-SR^9$ , protected OH (such as acyloxy), phenyl (Ph), substituted Ph,  $-OPh$ , substituted  $-OPh$ ,  $-NO_2$ ,  $-CN$ ,  $-NH_2$ ,  $-NHR^9$ ,  $-N(R^9)_2$ ,  $-NHCOR^9$ ,  $-NHCONHR^9$ ,  $-NHCON(R^9)_2$ ,  $-NR^9COR^9$ ,  $-NHCO_2R^9$ ,  $-CO_2R^9$ ,  $-CO_2H$ ,  $-COR^9$ ,  $-CONHR^9$ ,  $-CON(R^9)_2$ ,  $-S(O)_2R^9$ ,  $-SONH_2$ ,  $-S(O)R^9$ ,  $-SO_2NHR^9$ , or  $-NHS(O)_2R^9$ ; and

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

61. (currently amended) The compound according to claim 22 wherein Z is oxygen;

wherein  $R^2$  is:

~~i)  $CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CO_2H$ ; or~~  
 ~~$CH_2CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CH_2CO_2H$ ; and~~  
 ~~$CO_2H$ ,  $CH_2CO_2H$  or  $C_{1-6}$  alkyl esters,  $C_{3-10}$  cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more  $C_{1-6}$  alkyl groups optionally substituted with  $N(R)_2$  or 5-6 membered heterocyclic~~

rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

62. (currently amended) The compound according to claim 22 wherein Z is oxygen;

wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~  
~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and~~  
~~CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and~~

wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

63. (previously presented) The compound according to claim 22 wherein Z is oxygen; wherein  $R^3$  is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein  $R^4$  and  $R^5$  taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen,  $-R^9$ ,  $-OR^9$ ,  $-OH$ ,  $-SH$ ,  $-SR^9$ , protected OH (such as acyloxy), phenyl (Ph), substituted Ph,  $-OPh$ , substituted  $-OPh$ ,  $-NO_2$ ,  $-CN$ ,  $-NH_2$ ,  $-NHR^9$ ,  $-N(R^9)_2$ ,  $-NHCOR^9$ ,  $-NHCONHR^9$ ,  $-NHCON(R^9)_2$ ,  $-NR^9COR^9$ ,  $-NHCO_2R^9$ ,  $-CO_2R^9$ ,  $-CO_2H$ ,  $-COR^9$ ,  $-CONHR^9$ ,  $-CON(R^9)_2$ ,  $-S(O)_2R^9$ ,  $-SONH_2$ ,  $-S(O)R^9$ ,  $-SO_2NHR^9$ , or  $-NHS(O)_2R^9$ ; and

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group.

64. (currently amended) The compound according to claim 22 wherein Z is oxygen; wherein  $R^1$  is hydrogen,  $-R$ ,  $-CH_2OR$ ,  $-CH_2SR$ , or  $-CH_2Y$ ; wherein  $R^2$  is:

i)  ~~$CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CO_2H$ ; or~~  
 ~~$CH_2CO_2H$ , or an ester, or an amide thereof; or  $R^2$  is an isostere of said  $CH_2CO_2H$ ; and~~  
 ~~$CO_2H$ ,  $CH_2CO_2H$  or  $C_{1-6}$  alkyl esters,  $C_{3-10}$  cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary~~

amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and  
wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S.

65. (currently amended) The compound according to claim 22 wherein Z is oxygen;  
wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; wherein R<sup>2</sup> is:

i) CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or  
CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and  
CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic; and  
wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN,

$-\text{NH}_2$ ,  $-\text{NHR}^9$ ,  $-\text{N}(\text{R}^9)_2$ ,  $-\text{NHCOR}^9$ ,  $-\text{NHCONHR}^9$ ,  $-\text{NHCON}(\text{R}^9)_2$ ,  
 $-\text{NR}^9\text{COR}^9$ ,  $-\text{NHCO}_2\text{R}^9$ ,  $-\text{CO}_2\text{R}^9$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{COR}^9$ ,  $-\text{CONHR}^9$ ,  $-\text{CON}(\text{R}^9)_2$ ,  
 $-\text{S}(\text{O})_2\text{R}^9$ ,  $-\text{SONH}_2$ ,  $-\text{S}(\text{O})\text{R}^9$ ,  $-\text{SO}_2\text{NHR}^9$ , or  $-\text{NHS}(\text{O})_2\text{R}^9$ ; and  
wherein each  $\text{R}^9$  is independently selected from an  
aliphatic group or a substituted aliphatic group.

66. (previously presented) The compound according to  
claim 22 wherein  $\text{Z}$  is oxygen;  
wherein  $\text{R}^1$  is hydrogen,  $-\text{R}$ ,  $-\text{CH}_2\text{OR}$ ,  $-\text{CH}_2\text{SR}$ , or  $-\text{CH}_2\text{Y}$ ; wherein  $\text{R}^3$   
is a group having a molecular weight up to 140 Daltons  
selected from aliphatic, aryl, aralkyl, heterocyclyl or  
heterocyclalkyl ring wherein said heterocyclyl ring is a  
three to nine membered saturated or unsaturated mono-, bi-, or  
tri-heterocyclic ring system wherein each ring contains up to  
three heteroatoms selected from O, N, or S; and  
wherein  $\text{R}^4$  and  $\text{R}^5$  taken together with the intervening nitrogen  
form a mono-, bi- or tricyclic hetero ring system wherein each  
ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with  
one or more groups independently selected from halogen,  $-\text{R}^9$ ,  
 $-\text{OR}^9$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{SR}^9$ , protected OH (such as acyloxy), phenyl  
(Ph), substituted Ph,  $-\text{OPh}$ , substituted  $-\text{OPh}$ ,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  
 $-\text{NH}_2$ ,  $-\text{NHR}^9$ ,  $-\text{N}(\text{R}^9)_2$ ,  $-\text{NHCOR}^9$ ,  $-\text{NHCONHR}^9$ ,  $-\text{NHCON}(\text{R}^9)_2$ ,  
 $-\text{NR}^9\text{COR}^9$ ,  $-\text{NHCO}_2\text{R}^9$ ,  $-\text{CO}_2\text{R}^9$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{COR}^9$ ,  $-\text{CONHR}^9$ ,  $-\text{CON}(\text{R}^9)_2$ ,  
 $-\text{S}(\text{O})_2\text{R}^9$ ,  $-\text{SONH}_2$ ,  $-\text{S}(\text{O})\text{R}^9$ ,  $-\text{SO}_2\text{NHR}^9$ , or  $-\text{NHS}(\text{O})_2\text{R}^9$ ; and  
wherein each  $\text{R}^9$  is independently selected from an  
aliphatic group or a substituted aliphatic group.

67. (currently amended) The compound according to claim  
22 wherein  $\text{Z}$  is oxygen;  
wherein  $\text{R}^2$  is:

i)  ~~$\text{CO}_2\text{H}$ , or an ester, or an amide thereof; or  $\text{R}^2$  is an  
isostere of said  $\text{CO}_2\text{H}$ ; or~~

~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H;~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic;

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

68. (currently amended) The compound according to claim 22 wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~

~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H,~~  
CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic;

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

69. (currently amended) The compound according to claim 22 wherein Z is oxygen;  
wherein R<sup>1</sup> is hydrogen, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y; wherein R<sup>2</sup> is:

i) ~~CO<sub>2</sub>H, or an ester, or an amide thereof, or R<sup>2</sup> is an isostere of said CO<sub>2</sub>H; or~~

~~CH<sub>2</sub>CO<sub>2</sub>H, or an ester, or an amide thereof; or R<sup>2</sup> is an isostere of said CH<sub>2</sub>CO<sub>2</sub>H; and~~

CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl groups optionally substituted with N(R)<sub>2</sub> or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched C<sub>1-12</sub> aliphatic;

wherein R<sup>3</sup> is a group having a molecular weight up to 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclylalkyl ring wherein said heterocyclyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system wherein each ring of the system has 5-7 ring atoms;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

70. (previously presented) The compound according to claim 22 wherein R<sup>2</sup> is CO<sub>2</sub>H.

71. (previously presented) The compound according to claim 22 wherein R<sup>1</sup> is -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y.

72. (previously presented) The compound according to claim 71 wherein R<sup>1</sup> is -CH<sub>2</sub>Y.

73. (previously presented) The compound according to claim 72 wherein R<sup>1</sup> is -CH<sub>2</sub>F.

74. (previously presented) The compound according to claim 22 wherein R<sup>3</sup> is a C<sub>1-4</sub> alkyl group.

75. (previously presented) The compound according to claim 22 wherein R<sup>1</sup> is -CH<sub>2</sub>F and R<sup>3</sup> is a C<sub>1-4</sub> alkyl group.

76. (previously presented) The compound according to claim 22 wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a ring selected from isoindole, indoline, indazole, purine, dihydropyridine, benzimidazole, imidazole, imidazoline, pyrrole, pyrrolidine, pyrrolidine, pyrazole, pyrazoline, pyrazolidine, triazole, piperidine, morpholine, thiomorpholine, piperazine, phenothiazine, phenoxazine, dihydrophenazine, dihydrocinnoline, dihydroquinoxaline, tetrahydroquinoline, tetrahydroisoquinoline, dibenzoazepine, dihydro-dibenzoazepine, dihydronaphthyridine, tetrahydronaphthyridine, dihydroacridine,  $\beta$ -carboline, pyrido[4,3-b]indole, 2,3,9-triazafluorene, 9-thia-2,10-diazaanthracene, 3,6,9-triazafluorene, thieno[3,2-b]pyrrole, or dihydrophenanthridine;

wherein said ring is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

77. (previously presented) The compound according to claim 76 wherein R<sup>4</sup> and R<sup>5</sup> taken together with the intervening nitrogen form a ring selected from carbazole, phenothiazine, indole, indoline, 5H-dibenzo[b,f]azepine, 10,11-dihydro-5H-dibenzo[b,f]azepine,  $\beta$ -carboline, pyrido[4,3-b]indole, 2,3,9-triazafluorene, 9-thia-2,10-diazaanthracene, 3,6,9-triazafluorene, thieno[3,2-b]pyrrole, or dihydropheanthridine;

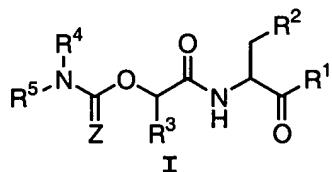
wherein said ring is optionally substituted with one or more groups independently selected from halogen, -R<sup>9</sup>, -OR<sup>9</sup>, -OH, -SH, -SR<sup>9</sup>, protected OH (such as acyloxy), phenyl (Ph), substituted Ph, -OPh, substituted -OPh, -NO<sub>2</sub>, -CN, -NH<sub>2</sub>, -NHR<sup>9</sup>, -N(R<sup>9</sup>)<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONHR<sup>9</sup>, -NHCON(R<sup>9</sup>)<sub>2</sub>, -NR<sup>9</sup>COR<sup>9</sup>, -NHCO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>R<sup>9</sup>, -CO<sub>2</sub>H, -COR<sup>9</sup>, -CONHR<sup>9</sup>, -CON(R<sup>9</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>9</sup>, -SONH<sub>2</sub>, -S(O)R<sup>9</sup>, -SO<sub>2</sub>NHR<sup>9</sup>, or -NHS(O)<sub>2</sub>R<sup>9</sup>; and

wherein each R<sup>9</sup> is independently selected from an aliphatic group or a substituted aliphatic group.

78. (previously presented) A pharmaceutical composition comprising a compound according to claim 22 and a pharmaceutically acceptable carrier.

79. (currently amended) A method of treating a caspase-mediated disease selected from an inflammatory disease, osteoarthritis, rheumatoid arthritis, psoriasis, glomerulonephritis, graft vs host disease, inflammatory bowel disease, sepsis, septic shock, burns, stroke, cerebral ischemia, traumatic brain injury, neurological damage due to stroke, spinal cord injury, amyotrophic lateral sclerosis, multiple sclerosis, myocardial infarct, myocardial ischemia, atherosclerosis, acute respiratory failure, adult respiratory

distress syndrome, pancreatitis, various forms of liver and renal disease, acute renal failure, an excess dietary alcohol intake disease, chronic active hepatitis, hepatitis B, hepatitis-C, or coronary artery bypass graft or a treatment for complications associated with coronary bypass grafts in a patient in need thereof that is alleviated by treatment with a caspase inhibitor, comprising administering to a said patient in need of such a treatment a therapeutically effective amount of a compound according to formula I:



wherein:

Z is oxygen or sulfur;

R<sup>1</sup> is hydrogen, -CHN<sub>2</sub>, -R, -CH<sub>2</sub>OR, -CH<sub>2</sub>SR, or -CH<sub>2</sub>Y;

R is a C<sub>1-12</sub> aliphatic, aryl, aralkyl, heterocyclyl, or heterocyclylalkyl ring, wherein each of these groups is optionally substituted, and wherein said heterocyclic ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S;

Y is an electronegative leaving group selected from F, Cl, Br, I, arylsulfonyloxy, alkylsulfonyloxy, trifluoromethanesulfonyloxy, OR', SR', -OC=O(R'), or -OPO(R<sup>6</sup>)(R<sup>7</sup>);

wherein R' is an aliphatic group, an aryl group, an aralkyl group, a carbocyclic group, an alkyl carbocyclic group, a heterocyclic group, or an alkyl heterocyclic group;  
wherein R<sup>6</sup> and R<sup>7</sup> are independently selected from R or OR;

R<sup>2</sup> is CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or C<sub>1-6</sub> alkyl esters, C<sub>3-10</sub> cycloalkyl esters, or cholesterol esters thereof; or primary, secondary or tertiary amides thereof; wherein suitable substituents on the nitrogen of said amides includes one or more C<sub>1-6</sub> alkyl

groups optionally substituted with  $N(R)_2$  or 5-6 membered heterocyclic rings containing 1-2 heteroatoms; and wherein R is linear or branched  $C_{1-12}$  aliphatic;

$R^3$  is selected from H, a side chain of a natural  $\alpha$ -amino acid, or a substituted or unsubstituted group having a molecular weight up to about 140 Daltons selected from aliphatic, aryl, aralkyl, heterocyclyl or heterocyclalkyl ring wherein said heterocyclyl or heterocyclalkyl ring is a three to nine membered saturated or unsaturated mono-, bi-, or tri-heterocyclic ring system wherein each ring contains up to three heteroatoms selected from O, N, or S; and

$R^4$  and  $R^5$  taken together with the intervening nitrogen form a mono-, bi- or tricyclic hetero ring system having 1-6 heteroatoms selected from nitrogen, oxygen or sulfur;

wherein said ring system is optionally substituted with one or more groups independently selected from halogen,  $-R^9$ ,  $-OR^9$ ,  $-OH$ ,  $-SH$ ,  $-SR^9$ , protected OH (such as acyloxy), phenyl (Ph), substituted Ph,  $-OPh$ , substituted  $-OPh$ ,  $-NO_2$ ,  $-CN$ ,  $-NH_2$ ,  $-NHR^9$ ,  $-N(R^9)_2$ ,  $-NHCOR^9$ ,  $-NHCONHR^9$ ,  $-NHCON(R^9)_2$ ,  $-NR^9COR^9$ ,  $-NHCO_2R^9$ ,  $-CO_2R^9$ ,  $-CO_2H$ ,  $-COR^9$ ,  $-CONHR^9$ ,  $-CON(R^9)_2$ ,  $-S(O)_2R^9$ ,  $-SONH_2$ ,  $-S(O)R^9$ ,  $-SO_2NHR^9$ , or  $-NHS(O)_2R^9$ ;

wherein each  $R^9$  is independently selected from an aliphatic group or a substituted aliphatic group;

wherein the optional substituents on said  $C_{1-12}$  aliphatic group or aryl, aralkyl, heterocyclyl, or heterocyclalkyl ring is independently selected from, from halogen,  $-R^{11}$ ,  $-OR^{11}$ ,  $-OH$ ,  $-SH$ ,  $-SR^{11}$ , acyloxy, substituted or unsubstituted Ph or OPh,  $-NO_2$ ,  $-CN$ ,  $-NH_2$ ,  $-NHR^{11}$ ,  $-N(R^{11})_2$ ,  $-NHCOR^{11}$ ,  $-NHCONHR^{11}$ ,  $-NHCON(R^{11})_2$ ,  $-NR^{11}COR^{11}$ ,  $-NHCO_2R^{11}$ ,  $-CO_2R^{11}$ ,  $-CO_2H$ ,  $-COR^{11}$ ,  $-CONHR^{11}$ ,  $-CON(R^{11})_2$ ,  $-S(O)_2R^{11}$ ,  $-SONH_2$ ,  $-S(O)R^{11}$ ,  $-SO_2NHR^{11}$ ,  $-NHS(O)_2R^{11}$ ,  $=O$ ,  $=S$ ,  $=NNHR^{11}$ ,  $=NNR^{11}_2$ ,  $=N-OR^{11}$ ,  $=NNHCOR^{11}$ ,  $=NNHCO_2R^{11}$ ,  $=NNHSO_2R^{11}$ , or  $=NR^{11}$ ; and

wherein each  $R^{11}$  is independently selected from a  $C_{1-12}$  aliphatic group or a substituted  $C_{1-12}$  aliphatic group.

80. (canceled)

81. (currently amended) A method for the preservation of cells in an organ for transplant or in a blood product said method comprising the step of bathing the cells in a solution of a compound ~~of formula I~~ according to claim 22.